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Upper respiratory tract diseases in captive orangutans (*Pongo abelii, Pongo pygmaeus*): prevalence in 20 European zoos and possible predisposing factors

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ZUSAMMENFASSUNG

Orang-Utans (*Pongo abelii, P. pygmaeus*) in Zoos zeigen häufig chronische Erkrankungen der oberen Atemwege, deren Ursache noch unbekannt ist. In dieser Studie wurde die Prävalenz von Atemwegserkrankungen bei Orang-Utans in europäischen Zoos bestimmt (201 Tiere in 20 Zoos) und prädisponierende Faktoren wurden untersucht. Borneo Orang-Utans (*P. pygmaeus*) zeigten signifikant öfter chronische Atemwegssymptome (13.8% der Tiere) als Sumatra Orang-Utans (*P. abelii*; 3.6%) und männliche Tiere öfter (15.8%) als weibliche (3.9%). Handaufgezogene Tiere entwickelten öfter Kehlsackinfektionen (21%) als durch ihre Eltern aufgezogene (5%). Oft waren erkrankte Tiere auch untereinander verwandt. Keine der untersuchten Umweltbedingungen (Gehegegrösse, -struktur, Klima, Menschenkontakt) hatte einen signifikanten Einfluss auf die Prävalenz der Erkrankungen. Individuelle Faktoren scheinen daher in der Pathogenese von Atemwegserkrankungen bei Orang-Utans von grösserer Bedeutung zu sein als die Umgebungsbedingungen in den Zoos. Um diese Erkrankungen in einem frühen und noch therapierbaren Stadium festzustellen, sollten insbesondere Borneo Orang-Utans, männliche und handaufgezogene Tiere, sowie Tiere mit erkrankten verwandten Tieren medizinisch genau überwacht werden.

SUMMARY

Chronic upper respiratory tract diseases are severe problems in captive orangutans (*Pongo abelii, P. pygmaeus*), but the etiology and pathogenesis are unknown. This study recorded the prevalence of such diseases in captive European orangutans (201 animals; 20 zoos) and investigated possible predisposing factors. Bornean orangutans (*P. pygmaeus*) showed chronic respiratory signs (13.8% of all animals) significantly more often than Sumatran (*P. abelii*; 3.6%), and male animals more often (15.8%) than females (3.9%). Hand-reared animals developed more air sacculitis (21%) than parent-reared animals (5%). Diseased animals were more often genetically related to animals with respiratory diseases (93%) than to healthy animals (54%). None of the environmental conditions investigated (enclosure size and structure, climate, human contact) had a significant effect on disease prevalence. The present results suggest a higher importance of individual factors, including inheritance, for the development of upper respiratory tract diseases than environmental conditions. Bornean, male and hand-reared orangutans and animals related to diseased animals need increased medical surveillance for an early detection of respiratory diseases at a possibly still curable stage.

UPPER RESPIRATORY TRACT DISEASES IN CAPTIVE ORANGUTANS *(PONGO ABELII, PONGO PYGMAEUS)*: PREVALENCE IN 20 EUROPEAN ZOOS AND POSSIBLE PREDISPOSING FACTORS

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ABSTRACT

Upper respiratory tract diseases are severe problems in captive orangutans (*Pongo abelii, P. pygmaeus*), but the pathogenesis is unknown. We recorded the prevalence of such diseases in captive European orangutans (201 animals; 20 zoos) and investigated possible predisposing factors. Bornean orangutans (*P. pygmaeus*) showed chronic respiratory signs significantly more often (13.8%) than Sumatran (*P. abelii*; 3.6%), and male animals more often (15.8%) than females (3.9%). Hand-reared animals developed more air sacculitis (21%) than parent-reared animals (5%). Diseased animals were more often genetically related to animals with respiratory diseases (93%) than to healthy animals (54%). None of the environmental conditions investigated had a significant effect on disease prevalence. Results suggest a higher importance of individual factors, including inheritance, for the development of upper respiratory tract diseases than environmental conditions. Bornean, male and hand-reared orangutans and animals related to diseased animals need increased medical surveillance for an early detection of respiratory diseases.

INTRODUCTION

Orangutans (*Pongo abelii, P. pygmaeus)* kept in zoos often suffer from upper respiratory tract diseases such as the common cold, sinusitis and air sacculitis [2, 4-6, 12, 21, 27, 34]. The latter affects the laryngeal air pouch, a unique anatomic feature in this and other primate species [15]. Several cases of air sacculitis have also been described in other primates, e.g. gorilla (*Gorilla gorilla*), chimpanzee (*Pan troglodytes*) and baboon (*Papio anubis*) [13, 14, 22, 35]. Interestingly, air sacculitis also occurred in orangutans kept in their natural habitat in Borneo [21]. Respiratory diseases in orangutans are often chronic and can even lead to death due to aspiration pneumonia or septicemia [12, 21, 27]. However, the exact etiology and pathogenesis of sinusitis and air sacculitis in orangutans or other primates are not completely understood. According to a widely accepted theory, a primary infection of the upper airways leads to continuous drainage of exudates into the air sacs, followed by a secondary infection at this location [5, 10, 21], because the air sacs are connected with the upper respiratory tract via two bilateral openings in the laryngeal cavity [12]. Most commonly involved microorganisms are gram-negative bacteria such as *Escherichia coli*, *Proteus* ssp., *Pseudomonas aeruginosa* and *Klebsiella pneumonia*, and mixed infections with *Streptococcus* ssp. and *Staphylococcus* ssp. have also been described [e.g. 6, 12, 21, 35]. Possible predisposing factors that have been previously discussed include fecal-derived infections due to overcrowding and contamination of the environment [5, 12, 17, 21], contact to human pathogens [17, 26], long-term antibiotic therapies altering the physiological bacterial flora in the airways [31], and a suppressed immune system [5, 9, 11].

It was the aim of this study to describe the prevalence of upper respiratory tract diseases in the orangutan population of zoological institutions on the basis of a selected subset of European facilities, and to determine possible predisposing factors and causes. Individual factors such

as species, gender, age, rearing history, family and medical history as well as housing conditions such as group size, enclosure structure, climate and human contact were assumed to have an influence on the development of upper respiratory tract diseases.

ANIMALS, MATERIAL AND METHODS

During 2009, 20 European zoological institutions holding Sumatran (*Pongo abelii*) or Bornean orangutans (*Pongo pygmaeus*) in Switzerland, Germany, France, Great Britain, Ireland and the Netherlands were visited for data collection. All orangutans living at the visited institutions between 1969 and 2009 were considered in this study, and data on individual animals and medical records were collected. The environmental conditions were evaluated in each visited zoo. The daily management routines were not disturbed and no harm was inflicted on any animal during the course of the study.

Individual factors

Individual factors potentially involved in predisposing animals for the disease included species, gender, age and rearing history. All orangutans of a zoo's total population from 1969 to 2009 were listed with their individual data, including transfers between zoos, as described in the zoos' specimen reports and the 2007 studbook data [3]. Hybrids were excluded from the analysis to associate the factor species with respiratory diseases. Individual ages referred to the current age of healthy animals or the age at death in animals that had not suffered from respiratory diseases, and in case of animals with respiratory disease it referred to the age at the start of clinical signs. Wild born animals with studbook entries stating unknown rearing history were assumed to be hand-reared, as wild orangutans are most often caught during infancy [29].

Medical history

Medical records of all orangutans between 1969 and 2009 with duration of more than one year were evaluated to determine a status of respiratory disease for each animal. Every event involving respiratory signs (nasal discharge, sneezing, coughing, colds and dyspnea) was listed with date, diagnosis and duration where possible, to detect any onset of chronic respiratory signs or the diagnosis of air sacculitis. Entries with an interval of seven days or more were understood as two different events. A status of respiratory disease was determined for each animal: (1) “air sacculitis”, if this diagnosis had been confirmed under anesthesia or at necropsy, (2) “chronic respiratory signs only”, if an animal never had a diagnosis of air sacculitis but at least three entries regarding respiratory diseases per year and/or if entries were not clearly separable from each other as different events, and (3) “healthy” for the remaining animals without or with only few (less than three events per year) respiratory signs. If available, results of bacterial investigations were noted. A total of 184 medical records were evaluated. In addition, eight animals were currently living at the zoos without any medical records but with a confirmed health status by veterinarians and keepers, and nine other, deceased animals showed signs of respiratory disease during necropsy. The latter were included in the analysis for individual factors. Therefore, a total of 201 animals were included in this study. The size of the group in which the animal lived at the onset of disease, and the number of other affected animals at this time, was noted if possible. These were considered individual factors because they were not the same for each animal in a given zoo. Finally, a genealogical tree was drawn for each animal. All family members (parents and grand-parents) were marked “healthy” or “with respiratory disease” if appropriate information was available from their medical records.

Further evaluation of the medical records included the total number of entries regarding any kind of disease (general entries), the number of events involving diarrhea, the number of

antibiotic therapies, and the number of anesthetic events. All events were counted and divided by the duration of the medical record in years, resulting in a mean number of events per year. The percentage of respiratory diseases of all general entries and the percentage of events involving diarrhea were additionally calculated (Table 1). Results were used to associate the medical history of each animal with the possible onset of respiratory disease. For animals with a “healthy” respiratory status, the whole medical record was evaluated. In animals with a respiratory disease defined as described above, only the part of the medical record prior to the start of disease was considered, because the factors potentially leading to the onset of disease were the focus of this investigation. The number of antibiotic therapies was additionally compared between animals with “chronic respiratory signs only” and animals with “air sacculitis” during the time of their disease. Records of 14 animals with respiratory disease could not be evaluated either because the entries immediately started with chronic respiratory signs, or because the exact start of signs remained uncertain. Therefore, the number of investigated animals did not equal 201 in every analysis. Medical records of 79 animals living longer than a year at any of the zoos between 1969 and 2009 were missing and could not be evaluated.

Environmental factors

Characterizing environmental conditions such as space, climate and contact to humans possibly leading to respiratory disease, was another aim of this study. Similar to the health status of individual animals described above, each status of a zoo was defined as “healthy” (all animals between 1969 and 2009 defined “healthy”, i.e. no cases of “chronic respiratory signs only” or “air sacculitis”), as “chronic signs only” (at least one case with chronic respiratory signs, but no case of air sacculitis) or as “air sacculitis” (at least one case of air sacculitis) and compared with the environmental factors measured. Although the climate in a

given enclosure may vary throughout the year, the difference between the visited zoos was assumed to stay approximately the same at any point in time. Therefore, climatic factors were also included in the study and compared between zoos with and without respiratory diseases. Nevertheless, the intention was to determine the environmental conditions at the start of upper respiratory tract diseases. Any subsequent changes in the environment of an animal with respiratory disease (e.g. a different enclosure) were not considered. This ensured that facilities where a diseased animal had arrived were not associated with the development of respiratory disease. Two zoos were therefore excluded from the analysis for environmental conditions, because the diseases of the respective animals had started in different enclosures than the current.

The area and volume of each enclosure were measured in m^2 and m^3, respectively (Table 2), and the presence or absence of an outdoor exhibit was noted. The type of enclosure floor (solid or natural, e.g. soil, bark mulch) was recorded for each zoo, and whether detergent or disinfectants were used for enclosure cleaning (yes/no). Possible contact to humans was evaluated regarding the boundary between enclosure and visitor area (closed by glass panes or open) and whether keepers suffering from a cold still worked in close contact with the apes or not. The temperature (ºC) and humidity (%) were logged at intervals of 30 minutes during 48-72 hours in close proximity of the indoor enclosures and overnight cages (Thermocron and Humidity Logger HC, OnSolution Pty Ltd, Baulkham Hills, Australia). The amount of ammonia in the air of the enclosures was measured at a height of approximately 1 meter above the floor (Accuro hand pump and ammonia 2/a tubes, 2-30 ppm, Draeger Safety, Dietlikon, Switzerland). To detect the amount of microorganism in the air, an air sampler (mas-100, MBV, Stäfa, Switzerland) was used with a sampled air volume of 10 l and unspecific agar plates (Isolator TSA, BD, Basel, Switzerland). The number of colony forming units was counted after 72 hours of incubation at room temperature. All climate

measurements (Table 2) were conducted in the morning before the first cleaning of the enclosure.

Statistical analyses

Data are presented as means with standard deviations. All quantitative data were tested for normal distribution using a Kolmogorov-Smirnov-Test. For differences between “healthy” groups (animals or zoos) and groups with “chronic respiratory signs only” or “air sacculitis” (animals or zoos), respectively, t-tests were used for normally distributed data and Mann-Whitney U-tests for factors not normally distributed between the groups. Qualitative individual and environmental factors consisting of categories were compared between the different groups by Yates corrected chi-square tests. The odds ratio was additionally calculated for groups with significant differences. All tests were two-tailed and significant p-levels were set at 0.05 for all tests.

RESULTS

Individual factors and respiratory disease

The Bornean species was represented with 40 % (n=80) of all animals and the Sumatran species with 56 % (n=112). Nine animals (4%) were hybrids. The distribution of the species between the visited zoos was equal: Bornean and Sumatran orangutans were each kept in 10 of the visited zoos. There were more female animals (62%, n=125) in the study population than males (38%, n=76). The age of all animals averaged 20 ± 12 years, with an equal age distribution between male and female animals (18.8 ± 11.8 and 21.7 ± 11.7, respectively) and Bornean and Sumatran animals (20.9 ± 11.7 and 20.1 ± 11.9, respectively). One hundred (49.8%) of all animals were hand-reared, 101 (50.2%) were parent-reared.

The duration of all medical records evaluated averaged 9.9 (± 8.1) years per animal. A status of “chronic respiratory signs only” could be determined in 15 animals (7.5 %), 26 animals (12.9 %) had a confirmed diagnosis of “air sacculitis” and the majority of animals (n=160; 79.6 %) were defined as “healthy”. The mean number of general entries (regarding any kind of disease) per year and animal was 1.6 (± 1.7) (Table 1). Respiratory signs were seen in 25.7% (± 29.3) of all entries, with signs regarding colds (congested nose, sneezing) being the most common entries, followed by cough and nasal discharge. Events involving diarrhea were counted in 27.2 % (± 29.3) of all events. The number of antibiotic therapies and anesthetic events averaged at 0.4 (± 0.6) and 0.3 (± 0.9) per animal and year, respectively (Table 1).

If respiratory diseases of the two species were compared, Bornean orangutans showed significantly more “chronic respiratory signs only” (13.8 %, n=11) compared to the Sumatran species (3.6%, n=4) (Chi^2 5.0, p = 0.026, Table 3). The calculated odds ratio to develop chronic respiratory signs in Bornean orangutans compared to Sumatran orangutans was 4.1 (95% CI 1.3-13.6). “Air sacculitis” occurred in 10 % (n=8) of the Bornean and 14.3 % (n=16) of the Sumatran animals; there was no significant difference between the species in this respect.

Males showed with 15.8 % (n=12) significantly more “chronic respiratory signs only” than females with 3.9 % (n=3) (Chi^2 11.0, p = 0.001) and had an 8.1 fold higher odds ratio for developing chronic respiratory signs than females (95% CI 2.2-29.8). There were not more males in the Bornean species (38.8%) than in the Sumatran species (36.6%) ($Chi^2$0.02, p = 0.880). “Air sacculitis” occurred equally in males (14.5%) and females (12%) (Table 3).

The age of the animals did not differ significantly between healthy animals and the two groups of animals with respiratory diseases (Table 3). The youngest animals with a status of “chronic respiratory signs only” or “air sacculitis” were 1 and 7 years old, respectively, and the oldest 42 and 33 years, respectively.

No difference could be detected between hand-reared and parent-reared animals in relation to "chronic respiratory signs only". However, hand-reared animals (21%, n=21) showed significantly more "air sacculitis" than parent-reared animals (5%, n=5) (Chi^2 9.7, p = 0.002, Table 3) and the odds ratio of hand-reared animals to develop air sacculitis compared to parent-reared animals was 5.0 (95% CI 1.8-13.9). The percentage of hand-reared animals did not significantly differ between the Bornean (51%, n=41) and the Sumatran species (49%, n=55) (Chi^2 0.02, p = 0.884) and a similar number of male animals (51%, n=39) was hand-reared as females (49%, n=61) (Chi^2 0.04, p = 0.841).

The group size of all animals averaged 7 ± 3 animals per group and was not significantly different between "healthy" animals, animals with "chronic signs only" and animals with "air sacculitis" (Table 3). Animals with respiratory diseases were in 66% (n=27) of all cases the only one in the whole group suffering from respiratory signs at the time of infection. In 17% (n=7) of all cases, one other animal was affected with respiratory signs at the same time and in 12% (n=5) two or more other animals were affected. In two animals (5%), the group at the time of onset of disease was not determinable.

The total number of general medical entries per year, episodes of diarrhea per year, number of antibiotic treatments per year and number of anesthetic events per year had no statistical significant influence on the development of "chronic respiratory signs only" or "air sacculitis" (Table 3). Animals with "chronic respiratory signs only" received an average of 0.16 antibiotic therapies per month between the start of signs and the end of the medical record. Animals with "air sacculitis" were treated with a mean of 0.21 antibiotic therapies per month between the onset of signs and the definite diagnosis. This difference was not significant (Mann-Whitney-U-test, p = 0.135). "Healthy" animals received an average of 0.2 (±0.4) antibiotic treatments per year and animal.

Bacterial investigations of exudates from nose and/or air sac were conducted in 26 of the 41 cases with respiratory disease. Most often, a mixed flora occurred with *Escherichia coli* (in 65%, n=17, of all cases), *Pseudomonas aeruginosa* (62%, n=16), *Klebsiella pneumonia*e (35%, n=9), *Streptococcus* ssp. (35%, n=9), *Proteus* ssp. (23%, n=6), and *Staphylococcus* ssp. (19%, n=5) representing the most common bacteria found.

The respiratory status of the parents was known in 46% (n=92) of all animals, which were therefore included in the genealogical analysis. Of 93% (n=14) of all animals with "chronic respiratory signs only" or "air sacculitis" also one or more parents had a respiratory disease, while healthy animals had significantly less often at least one parent with respiratory disease (54%, n=42) (Chi^2 6.4, p = 0.012).

Environmental factors and respiratory disease

Cases of "chronic respiratory signs only" without any cases of "air sacculitis" were determined in a total of 3 of the 20 zoos and a total of 12 of the 20 zoos had cases of "air sacculitis". Five of the 20 zoos were defined as "healthy" because they had neither animals with "chronic respiratory signs only" nor animals with "air sacculitis".

The indoor enclosure area of the 20 zoos averaged 154 m^2 (± 136) and the mean indoor volume was 807 m^3 (± 1071). Two zoos had no outdoor exhibit. The floor of the indoor enclosures consisted of natural material in 7 of the 20 zoos. Eleven zoos used detergents or disinfectants for cleaning. The visitor area was open toward the orangutan enclosure in 4 of the 20 zoos and in 16 zoos keepers still worked with orangutans when suffering from a cold. The climatic factors in the visited zoos averaged 22.0° Celsius (± 2.2) temperature, 63.6% (± 10.7) relative humidity, 1 ppm (± 1.6) ammonia and 212.3 microorganisms per 10 liters of air (± 250.3). All measured indoor enclosure sizes and climatic factors are shown in Table 2.

The area and volume of the enclosures were not significantly different between “healthy” zoos, zoos with “chronic respiratory signs only” and zoos with “air sacculitis” (Table 4). Also none of the climatic factors significantly differed between “healthy” zoos and the two other zoo groups (Table 4). The presence or absence of outdoor exhibits, the kind of enclosure floor, and cleaning with or without detergent did not have any effect on the respiratory disease status of the zoos. Also open visitor areas and whether keepers were allowed to continue working while suffering from a cold did not have any significant influence (Table 4).

DISCUSSION

The present study investigated the prevalence of chronic respiratory signs and air sacculitis in 201 orangutans of 20 European zoos between 1969 and 2009 and individual and environmental factors possibly involved in the development and expression of these diseases. Of all animals, 20.4% had either “chronic respiratory signs only” or “air sacculitis” and these diseases accounted for one fourth of all medical entries in general. Considering the 79 animals with unknown respiratory status due to missing medical records, the percentage of animals with respiratory disease could even be greater. Only in 5 of the 20 visited zoos, no respiratory diseases had occurred at all. Upper respiratory tract diseases thus proved to be a severe problem in the captive orangutan population and the search for predisposing factors and causes seems justified. The present results revealed a high importance of individual factors, whereas environmental conditions appear less important in the occurrence of upper respiratory tract diseases in captive orangutans.

The evaluation of the medical records was limiting the study insofar that entries were not always clearly attributable to a certain event and medical records were kept differently at the different zoos. Nonetheless, the use of the present classification system of three different respiratory states seemed reliable enough, as the authors’, keepers’ and veterinarians’

subjective observations were always in agreement with the evaluated respiratory status of the animals. A total separation of the two groups “chronic respiratory signs only” and “air sacculitis” could be misleading, as air sacculitis included a preceding period of chronic respiratory signs in many cases. We had previously suggested that chronic sinusitis could secondarily lead to air sacculitis in orangutans [41], although the exact diagnosis of sinusitis in orangutans remains difficult because a computed tomography scan (CT) is needed for an exact evaluation of the head [1, 39, 42]. The respiratory signs entered most commonly in the medical records of the orangutans in this study included colds, congested nose, sneezing, coughing and nasal discharge, which are signs most often occurring in cases of sinusitis in humans [20, 23, 24]. Sinusitis can therefore be assumed in orangutans showing chronic reoccurring respiratory signs, and a CT of the head could be used to confirm the diagnosis. It remains to be investigated whether all animals with chronic respiratory signs at present are going to develop air sacculitis at a later point in time.

Bornean orangutans developed chronic respiratory signs significantly more often than Sumatran animals. The skull of the Sumatran orangutan has been described with a straight diagonal profile of the face compared to a concave form of the face in the Bornean species [32]. The thus possibly narrowed intra- and paranasal cavities and drainage pathways in Bornean orangutans could explain the higher susceptibility of this species to chronic respiratory signs, as anatomic variations within the nasal and paranasal cavities are also known to predispose humans for sinusitis and thus chronic respiratory signs [8, 39, 40]. Furthermore, obesity in primates has been suggested as predisposing factor for respiratory infections, because obese animals are more lethargic, move less and the clearance of respiratory secretions is thus impaired [5, 22]. Bornean orangutans in captivity tend to be more obese than the Sumatran species [32], an observation also made subjectively by the

authors in the present study population. This may also contribute to the higher incidence of "chronic respiratory signs" in the Bornean species.

Male animals also showed "chronic respiratory signs" significantly more often than females. Males of both species were equally represented in this study and results could therefore not have been skewed due to an overrepresentation of Bornean males. Studies in humans have investigated the influence of gender on respiratory tract diseases, but the divergent effects depending on the kind of disease prevented a valid conclusion. Macintyre et al. [25] found no significant difference in reported flu and sinusitis signs between the two genders. A computed tomography study of orangutan skulls by Koppe et al. [19] revealed a sexual dimorphism in the growth pattern of the maxillary sinus: in males, the maxillary sinus grows for a longer time than in females and is, once it has reached its full size, also larger than in females. Whether this could have an influence on the development of chronic respiratory signs cannot be ensured, because the size and shape of the openings between sinus and nasal cavity functioning as drainage pathways seem of higher importance for the development of sinusitis than the size of the sinus itself. The incidence of "air sacculitis" showed no significant difference between the two species and the two genders, which is consistent with findings of Lawson et al. [21], who reported air sacculitis in 14 juvenile Bornean orangutans of both genders. This suggests again a primary effect of chronic respiratory diseases in general, regardless of a later development of the specific condition "air sacculitis".

The age did not significantly differ between healthy animals and animals of the two groups with respiratory diseases. However, according to the present results, chronic respiratory signs appeared to occur earlier in life than air sacculitis. Air sacculitis has not been diagnosed in animals with a body weight of less than 13.6 kg, possibly due to the still small size of the air sacs in very young animals [21]. This finding again supports the hypothesis that air sacculitis is always preceded by chronic respiratory signs, for example due to sinusitis, and that these

two diseases could be causally associated. Consistently, 50% of the orangutans diagnosed with air sacculitis in the study of Lawson et al. [21] suffered from upper respiratory tract infections in the six months prior to diagnosis. The most commonly found microorganisms in animals with respiratory diseases in the present study were ubiquitous bacteria or part of the physiological flora of skin, respiratory and gastrointestinal tract. Their role in pathogenesis is less likely primary but rather causing opportunistic secondary infections. Viral infections of the upper respiratory tract have been suggested to predispose for secondary bacterial manifestations [16, 21] and decreased immune functions in individual animals due to various social and environmental factors may be associated with a higher risk for respiratory disease [e.g. 28]. Other diseases in the medical history of the animals did not seem to influence the development of "chronic respiratory signs" in general or "air sacculitis". The total medical entries gave an insight into an animal's overall health, but no association between other health problems and respiratory diseases could be found. Diarrhea has been associated with stress in primates [36], which is also known to reduce immune functions and can even predispose animals for respiratory disease [7, 30]. However, animals with respiratory diseases did not suffer significantly more often from diarrhea than other animals. Nonetheless, diarrhea is a very common problem in captive orangutans (27.2 % of all medical entries) and needs more detailed investigations. Anesthesia was thought to represent a stressor for animals and could therefore also lead to a reduction of immune functions. However, a recent review in human medicine showed that effects of anesthesia can be various depending on the anesthetic agent used, but the overall interactions between anesthesia and the immune system are rather minor and transient [33]. No causal relation could be found between the respiratory disease status of an animal in this study and the number of anesthesias it underwent before. Antibiotic treatments have been suggested to alter the bacterial flora in the respiratory tract and thus lead to infections in the air sac [31]. This hypothesis could not be supported either in the present

study, because the number of antibiotic treatments did not significantly differ for healthy animals or animals with respiratory disease during the time before the onset of disease. Also when the number of antibiotic therapies after the onset of disease was compared between animals with “chronic respiratory signs only” and animals with “air sacculitis”, the latter did not receive more antibiotic treatments compared to the former. A possible harmful effect of the length of antibiotic therapies could not be investigated in this study, because the exact duration of therapies very often remained unclear in medical records.

Of all individual factors, only the rearing history had a significant effect on air sacculitis. More hand-reared animals were diagnosed with air sacculitis than parent-reared animals. As stated above, air sacculitis does not occur until a certain age and it therefore seems unlikely that any events during the time of hand-rearing, e.g. contact to human pathogens, are directly associated with its development. This association between hand-rearing and air sacculitis could therefore also indicate a report bias in the data as stated above, as observations in the medical records were sometimes unclear or incomplete. Perhaps orangutan-specific pathogens play a role, for which hand-reared orangutan infants did not develop sufficient immunity, or reduced immune functions predispose them for disease possibly due to stress, since hand-reared animals are often overwhelmed with the normal behavior among conspecifics in the group. Also contact to people during later life could predispose these animals for infections, as hand-reared animals often search closer contact to humans than parent-reared animals (keepers’ and personal observation). The danger of possible transmission of respiratory pathogens between humans and apes in the wild has often been described [18, 37, 38]. In zoo settings this could be of even greater importance, where animals often live in close contact to keepers and visitors. However, no association between contact to humans (keepers with colds, visitors) and the incidence of chronic respiratory signs only or air sacculitis could be detected in this study.

Overcrowding can also increase the susceptibility to and transmission of diseases in orangutans [17] and the resulting fecal contamination of the environment has been suggested as predisposing factor for air sacculitis [5, 12]. However, neither the area, nor the volume of the enclosures, nor the group size at the time of infection nor the investigated cleaning management, nor the ground material of the enclosure seemed to play a role in the development of respiratory diseases in this study. In addition, the percentage of animals with respiratory diseases per group was small, as in the majority of all cases only one animal per group was affected at a given time. This finding underlines again the higher importance of individual factors compared to environmental conditions in the enclosure, which would be more likely to affect a greater percentage of animals in a group. However, the exact group density at time of infection could not be investigated due to lack of data, as it was difficult to retrospectively determine the exact number of animals living in a given enclosure size at any point in time. Therefore, only the total area and volume were used for analysis. Even though the climatic factors might vary over time, the differences between the zoos were assumed to stay approximately the same and thus comparable for the present analysis of zoos with and without respiratory diseases. To exclude the influence of severe changes in the environment, two zoos were not included in the study because respiratory diseases had started in different enclosures than the present.

Considering that none of the environmental factors investigated in this study showed any significant effects on upper respiratory tract diseases, we conclude that individual factors are of a much higher importance than environmental conditions for the development of respiratory disease. In human medicine, the pathogenesis of sinusitis is multifactorial, including inherited individual factors such as anatomic variations and ciliar dysfunctions [20, 24]. An inheritance of genetic predisposing factors increasing the susceptibility to respiratory disease also needs to be considered in orangutans, as almost all animals with respiratory

disease had a parent with respiratory disease as well. That this is not due to their simultaneous housing in the same zoo and group cannot be completely ruled out, but seems less likely since housing conditions were not significantly associated with any respiratory status group.

Conclusion

The results of the present study cannot reduce the possible causes for sinusitis and air sacculitis in orangutans to a single specific explanatory factor, indicating the complex multi-factorial pathogenesis of these diseases. If housing conditions played a role - which could not be shown in this study - their importance would definitely not be the same for each animal, as an onset of respiratory diseases depends strongly on individual predisposing factors increasing the susceptibility of an animal to disease. The role of suppressed immune functions in certain animals, e.g. due to high glucocorticoid levels following stressful events, malnutrition or possibly inherited cellular immunodeficiencies, still needs further investigations. Based on the present results, Bornean, male and hand-reared orangutans should receive increased medical surveillance to detect respiratory diseases at an early and thus still curable stage, especially if also closely related animals showed respiratory signs. Perhaps breeding animals with respiratory diseases and hand-rearing their offspring should even be discouraged to reduce the incidence of these harmful diseases in captive orangutans.

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Table 1. Medical issues of orangutans *(Pongo abelii, Pongo pygmaeus)* per year and group in 20 European zoos (1969 – 2009).

Zoo	Medical records	Duration (years)	General entries (n)	Respir. disease (%)	Diarrhea (%)	Antibiotic Therapies (n)	Anesthesias (n)
	n	Mean ± SD					
A	4	17.3 ± 7.7	1.3 ± 1.5	28 ± 28	28 ± 20	0.4 ± 0.2	0.4 ± 0.1
B	23	10.4 ± 7.4	1.5 ± 1.8	34 ± 23	17 ± 18	0.3 ± 0.3	0.2 ± 0.3
C	7	6.9 ± 4.8	2.5 ± 1.8	19 ± 26	60 ± 27	1.0 ± 1.4	0.3 ± 0.3
D	6	6.6 ± 2.7	0.5 ± 0.3	34 ± 44	2 ± 5	0.3 ± 0.3	0.4 ± 0.3
E	4	9.5 ± 5.2	3.0 ± 4.0	19 ± 26	35 ± 29	1.3 ± 1.3	0.1 ± 0.1
F	7	3.7 ± 1.3	0.6 ± 0.3	38 ± 45	17 ± 22	0.2 ± 0.2	0.1 ± 0.2
G	16	10.8 ± 11.4	2.0 ± 1.8	21 ± 21	33 ± 25	0.6 ± 0.7	0.4 ± 1.0
H	7	9.0 ± 4.9	2.2 ± 2.1	39 ± 29	19 ± 28	0.6 ± 0.2	0.5 ± 0.3
I	13	8.3 ± 5.7	0.7 ± 1.0	36 ± 39	19 ± 31	0.2 ± 0.4	0.1 ± 0.2
J	5	10.2 ± 7.7	0.3 ± 0.3	54 ± 41	17 ± 24	0.2 ± 0.2	0.1 ± 0.1
K	12	6.0 ± 4.9	1.6 ± 1.8	16 ± 37	38 ± 38	0.9 ± 1.4	1.6 ± 2.8
L	3	1.7 ± 0.2	2.8 ± 1.9	0 ± 0	56 ± 51	0.8 ± 0.3	0.0 ± 0.0
M	13	12.4 ± 8.1	0.9 ± 0.9	24 ± 28	28 ± 28	0.3 ± 0.3	0.1 ± 0.2
N	8	7.8 ± 5.4	4.4 ± 2.3	39 ± 28	17 ± 27	0.6 ± 0.5	0.1 ± 0.2
O	4	4.1 ± 4.1	2.5 ± 0.8	13 ± 16	45 ± 24	0.0 ± 0.0	0.0 ± 0.0
P	9	21.1 ± 15.2	0.6 ± 0.4	20 ± 13	34 ± 33	0.3 ± 0.2	0.2 ± 0.1
Q	6	7.5 ± 3.9	2.5 ± 2.1	48 ± 29	0 ± 0	0.7 ± 0.8	0.9 ± 0.8
R	8	10.3 ± 5.6	0.7 ± 0.5	14 ± 24	6 ± 18	0.3 ± 0.2	0.4 ± 0.2
S	13	12.1 ± 7.5	0.9 ± 0.9	4 ± 14	42 ± 38	0.4 ± 0.5	0.1 ± 0.1
T	16	11 ± 8.5	2.0 ± 1.4	19 ± 25	46 ± 25	0.1 ± 0.1	0.3 ± 0.4

Table 2. Size and climatic factors of inside enclosures for orangutans (*Pongo abelii*, *Pongo pygmaeus*) in 20 European zoos.

Zoo	Area (m^2)	Volume (m^3)	Temperature (°C) (Mean ± SD)	Humidity (%) (Mean ± SD)	Ammonia (ppm)	Bacteria (CFU/10l)
A[1]	225	900	20.7 ± 1.0	69.9 ± 5.9	0.0	154
B[1]	84	672	21.7 ± 0.9	71.3 ± 9.9	1.1	105
C[1]	112	448	21.8 ± 1.1	51.2 ± 5.5	1.0	43
D[2]	265	1155	23.1 ± 1.5	44.0 ± 6.4	0.1	289
E[2]	55	164	22.4 ± 1.1	63.5 ± 5.7	7.0	43
F[1]	45	226	19.5 ± 1.2	73.2 ± 5.6	1.8	247
G[2]	109	382	24.7 ± 0.6	57.1 ± 8.1	0.0	81
H[1]	90	360	21.1 ± 0.8	73.2 ± 5.6	1.2	55
I[1]	339	1697	22.6 ± 1.7	69.7 ± 6.3	0.0	72
J[1]	51	278	19.2 ± 0.8	75.9 ± 7.0	0.0	212
K[1]	236	1181	25.1 ± 4.3	60.1 ± 11.5	0.0	123
L[1]	600	5000	23.8 ± 1.5	49.9 ± 5.8	1.5	39
M[1]	200	600	20.7 ± 1.2	64.3 ± 5.6	2.5	806
N[1]	160	960	19.6 ± 0.8	81.8 ± 13.0	0.0	628
O[2]	56	168	20.6 ± 0.5	66.9 ± 4.2	0.0	156
P[2]	72	400	21.2 ± 1.2	76.4 ± 9.4	1.3	835
Q[1]	23	81	28.2 ± 1.3	47.1 ± 6.2	1.3	14
R[2]	99	394	20.0 ± 0.7	53.7 ± 13.8	1.3	58
S[1]	66	297	22.6 ± 1.4	56.7 ± 7.1	0.0	36
T[2]	195	781	21.3 ± 1.9	65.2 ± 8.2	0.1	249

[1] All animals housed in the same enclosure, [2] Animals housed in different enclosures

Table 3. Individual factors possibly influencing the incidence of "chronic respiratory signs only" (without air sacculitis) or "air sacculitis" in captive orangutans (*Pongo abelii*, *Pongo pygmaeus*) (n=170-201) of 20 European zoos, with respective data available from 1969 to 2009.

Individual factors		Total animals	Healthy	Chronic signs only	Air sacculitis	Test	Chronic signs only	Air sacculitis
			Animals (n)				p	
Species	P.pygmaeus	80	61	11	8	Chi^2	0.026	0.700
	P.abelii	112	92	4	16			
Sex	Male	76	53	12	11	Chi^2	0.001	0.489
	Female	125	107	3	15			
Rearing	Hand	100	73	6	21	Chi^2	0.883	0.002
	Parent	101	87	9	5			
			[1]Mean ± SD, [2]Median ± quartile range					
[1]Age		180	20.1 ± 11.8	16.7 ± 13.8	19.1 ± 13.2	T	0.360	0.801
[2]Medical entries/year		170	0.9 ± 1.3	0.5 ± 1.0	0.5 ± 1.2	U	0.206	0.471
[2]Diarrhea/year		170	0.2 ± 0.6	0.0 ± 0.2	0.3 ± 0.3	U	0.117	0.702
[2]Antibiotics/year		170	0.2 ± 0.4	0.2 ± 0.4	0.4 ± 0.5	U	0.900	0.780
[2]Anesthesias/year		170	0.2 ± 0.3	0.1 ± 0.4	0.0 ± 0.2	U	0.860	0.159
[2]Group size		180	7.0 ± 3.5	8.0 ± 5.0	7.0 ± 4.0	U	0.437	0.919

Chi^2 = Yates corrected chi-square test, T = t-test, U = Mann-Whitney U-Test

Table 4. Environmental factors of orangutan (*Pongo abelii*, *Pongo pygmaeus*) enclosures in 20 European zoos, possibly influencing the incidence of "chronic respiratory signs only" or "air sacculitis".

Environmental factors		Total zoos	Healthy	Chronic signs only	Air sacculitis	Test	Chronic signs only	Air sacculitis
			Zoos (n)				p	
Enclosure floor	Natural	6	2	0	4	Chi^2	0.673	0.576
	Solid	12	3	3	6			
Outdoor exhibit	Yes	16	5	3	8	Chi^2	0.715	0.788
	No	2	0	0	2			
Cleaning with detergent	Yes	10	3	2	5	Chi^2	0.572	0.855
	No	8	2	1	5			
Open visitor area	Yes	4	2	0	2	Chi^2	0.673	0.836
	No	14	3	3	8			
Keepers with colds work	No	3	2	1	0	Chi^2	0.572	0.180
	Yes	15	3	2	10			
			Mean ± SD					
Area (m^2)		18	222.5 ± 243.9	68.3 ± 14.6	130.3 ± 74.0	T	0.330	0.278
Volume (m^3)		18	1498.2 ± 2055.2	377.7 ± 263.4	543.9 ± 330.4	T	0.398	0.161
Temperature (°C)		18	21.5 ± 1.7	22.2 ± 0.5	22.0 ± 2.8	T	0.543	0.762
Humidity (%)		18	67.2 ± 10.3	63.8 ± 7.3	61.3 ± 12.8	T	0.638	0.389
Ammonia (ppm)		18	0.9 ± 0.9	2.7 ± 3.8	0.8 ± 0.8	T	0.327	0.721
Microorganisms (CFU/10l air)		18	269.8 ± 326.1	61.3 ± 38.0	243.5 ± 270.1	T	0.326	0.870

Chi^2 = Yates corrected chi-square test, T = t-test

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